REMARKS

This Amendment is in response to the Office Action mailed July 10, 2007. New claims 98-100 have been added. Claims 27 and 35 have been amended. Accordingly, Claims 27, 35 and 98-100 remain pending. Reconsideration is respectfully requested.

Claim Objections

In the Office Action, the examiner objects to claim 27 because the term "administered in the presence or not" is improper. Claim 27 has been amended to delete the phrase.

The examiner also objects to claim 35 because it is not clear what the term VSSP stands for and the phrase "administered in the presence of or incorporated into" is improper. Claim 35 has been amended to "very small size particle" and the phrase "administered in the presence of or incorporated into" has been deleted.

The disclosure is objected to by the examiner for failure to supply a sequence listing identifier to all disclosed sequences. Pursuant to 37 CFR §§ 1.821-1.825, applicants are electronically submitting herewith a Sequence Listing as a text file (.txt). The content of the sequence listing does not extend beyond the original disclosure and does not include new matter.

The examiner has also objected to the disclosure due to certain informalities. These informalities, including the sentence on page 6, line 4; page 8, line 37; page X, line Y; page 15, line 10; and "SEQ ID" rather than "SEQ ID NO:" throughout, have been corrected.

The disclosure is further objected to, by the examiner, due to the inclusion of a hyperlink. Applicants thank the examiner for pointing out the embedded hyperlink and have removed the hyperlink from the disclosure.

Accordingly, in light of the amendments to the specification, withdrawal of the objections is respectfully requested.

Rejections Under 35 U.S.C. §112, first paragraph

In the Office Action, the examiner rejects claims 27 and 35 under 35 U.S.C. 112, first paragraph, because, according to the examiner, the specification is does not enable any immunogenic composition comprising any VEGFR2 fragments and any mutant of any VEGF polypeptide. The examiner also states that the specification does not enable any VEGF and any VEGFR-2 fragments for use as an immunogen for inducing the production of antibodies and VEGF and VEGFR-2 specific cytotoxic CD8+ lymphocytes to treat cancer.

The claims, as amended, no longer refer to any VEGF polypeptide, but rather a VEGF-A polypeptide mutated to prevent binding to its receptor. Support for this amendment may be found, for example, on page 9, lines 27-29 and page 20, line 18.

Applicants have also amended claim 27, to further specify VEGFR-2 polypeptide fragments corresponding to the third, or first through third, terminal domains. Support for this amendment may be found, for example, on page 21, lines 9-15, and page 23, lines 17-24.

Claim 35 has been amended to state that the VEGF polypeptide has been mutated to prevent binding to its receptor. Support for this amendment can be found, for example, on page 9, lines 27-29 and page 20, line 18.

Accordingly, in light of the above remarks, applicants respectfully request that the examiner reconsider and withdraw the rejections under 35 U.S.C. §112, first paragraph.

The examiner also rejects claims 27 and 35 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification

in such a way as to reasonably convey to one skilled in the are that the inventor had possession of the claimed invention at the time the application was filed. More precisely, the examiner states that the specification does not provide a written description of any mutant of any VEGF for the claimed immunogenic composition, that induce VEGF-A specific antibody and VEGF-A specific CTL immune response in vivo to treat cancer.

As stated above, claim 27 has been amended to further define both the VEGF-A polypeptide, and the VEGFR-2 polypeptides. In addition, claim 35 has been amended to further define the VEGF polypeptide as being mutated to prevent binding to its receptor.

Applicants respectfully submit that these amendments would convey to one skilled in the art that Applicants had possession of the invention at the time of filing.

In the amended claims, Applicants are not claiming "any mutant," but only the use of VEGF-A specifically mutated in such a way as to prevent binding to VEGFR. Furthermore, not all forms of VEGFR are claimed but only VEGFR-2 polypeptide fragments corresponding to the first through third extracellular domains.

Accordingly, in light of the above remarks, applicants respectfully request that the examiner reconsider and withdraw the rejections under 35 U.S.C. §112, first paragraph.

Rejection Under 35 U.S.C. §102(b)

In the Office Action, the examiner rejects claim 27 as being anticipated by WO 99/45018 to Hicklin et al. (Hicklin). According to the examiner, the publication teaches an immunogenic composition for active immunization against angiogenesis associated antigens wherein the reference composition comprises immunogens, such as VEGF or an antigenic fragment thereof, and KDR/flk-1 (VEGFR2) and an antigenic fragment thereof, in the presence of a pharmaceutically acceptable adjuvant.

Applicants respectfully disagree. Hicklin discloses an anti-idiotypic antibody for active immunization against angiogenesis associated antigens. The antibody binds to the VEGF receptors such as KDR. Hinklin discloses treatment with an immunogen that causes an immune response against VEGF or KDR. In contrast, Applicants' invention claims immunotherapy with VEGF mutated at the VEGFR binding site, VEGFR-2 fragments corresponding to the first through third extracellular domains, or combinations thereof. Hinklin discloses neither the use of VEGF mutated to prevent binding at its receptor, nor the use of VEGFR-2 polypeptide fragments corresponding to the third or first through third extracellular domains.

As stated above, claim 27 as amended includes VEGF-A polypeptides mutated to prevent binding at its receptor, and VEGFR-2 polypeptide fragments corresponding to the third or first through third extracellular domains. Hinklin discloses neither VEGF-A mutated to prevent binding at its receptor site nor VEGFR-2 polypeptide fragments corresponding to the third or first through third extracellular domains. Therefore, Hinklin does not anticipate Applicants' invention.

Accordingly, in light of the above remarks, applicants respectfully request that the examiner reconsider and withdraw the rejection under 35 U.S.C. §102(b).

Rejection Under 35 U.S.C. §103(a)

In the Office Action, the examiner rejects claim 35 as unpatentable over WO 99/45018 to Hicklin et al. (Hicklin), in view of U.S. Patent No. 6,149,921 to Rodriguez et al. (Rodriguez). According to the examiner, Hicklin discloses an immunogenic composition for active immunization against angiogenesis associated antigens, where the reference composition comprises immunogens such as VEGF or antigenic fragments thereof, and KDR/flk-1 (VEGFR2) and antigenic fragments thereof, combined with a pharmaceutically acceptable adjuvant. The examiner concedes that Applicants' invention differs from the disclosure of (Hicklin) "in that immunogenic composition comprising VEGFR-2 polypeptide or fragments thereof

and a mutant of VEGF polypeptide (immunogenic fragment) in the presence of or incorporated into Neisseria meningitides outer membrane very small particles (VSSP) instead of adjuvant particles such as aluminum oxide or bacterial adjuvant BCG know in the art."

According to the examiner, "[t]he '921 patent teaches very small particle from the outer membrane complex of *N meningitides* as adjuvant for an immunogenic composition to elicit an immunogenic response against self antigens." The examiner then concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute *N meningitides* for known adjuvant particles.

As stated above, Hinklin discloses neither the use of VEGF mutated to prevent binding at its receptor, nor the use of VEGFR-2 polypeptide fragments corresponding to the third or first through third extracellular domains.

Also as stated above, claim 35 has been amended to state that the VEGF polypeptide has been mutated to prevent binding to its receptor. According to MPEP 706.02(j) "the prior art reference (or references when combined) must teach or suggest all the claim limitations." Since Hinklin does not disclose VEGF polypeptides mutated to prevent binding to its receptor, it would not be obvious to use the VSSP from *N Meningitides* disclosed in U.S. Patent No. 6,149,921 as an adjuvant for VEGF polypeptides mutated to prevent binding to its receptor.

Accordingly, in light of the above remarks, applicants respectfully request that the examiner reconsider and withdraw the rejection under 35 U.S.C. §103.

New Claims

New claims 98, 99, and 100, have been added. Claim 98 depends from claim 27 and specifically claims a mutant of $VEGF_{121}$. Support new claim 98 may be found, for example, on page 20, lines 18-32.

New claim 99 depends from claim 35, and specifically claims a mutant of $VEGF_{121}$. Support for new claim 99 may be found, for example, on page 20, lines 18-32.

New claim 100 also depends from claim 35 and specifically claims VEGFR-2 corresponding to the first through third extracellular domains. Support for new claim 100 may be found, for example, on page 21, lines 9-15.

Conclusion

In view of the above amendments and remarks, allowance of the pending claims is earnestly requested. If the examiner has any questions or concerns regarding this matter, she is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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